

# Treatment and Follow-Up Recommendations in Acute Respiratory Distress Syndrome Due to COVID-19 Infection

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## ABSTRACT

The actual incidence of hypoxic respiratory failure in the novel coronavirus disease 2019 (COVID-19) patients is not yet clear. It was reported that approximately 14% of COVID-19 patients have severe disease requiring oxygen treatment, 5% need intensive care unit (ICU) admission and mechanical ventilation (MV). In these patients acute respiratory distress syndrome (ARDS) is the main problem that requires careful and comprehensive strategies of treatment in order to prevent mortality. In this short review, guidelines about COVID-19 treatment were evaluated and a summary of recommendations and their explanations were made for the treatment and follow-up of ARDS due to COVID-19 infection.

**Key words:** COVID-19, Respiratory Failure, ARDS, Hypoxia, Mechanical Ventilation

## Introduction

The actual incidence of hypoxic respiratory failure in COVID-19 patients is not yet clear. However, in a study from China, it was reported that approximately 14% of COVID-19 patients have severe disease requiring oxygen treatment, 5% need ICU admission and the majority of critically ill patients with COVID-19 receive MV (1). Dyspnea is the most common symptom of severe disease and is often accompanied by hypoxemia (2). Patients with severe COVID-19 commonly meet the criteria of acute respiratory distress syndrome (ARDS) that is defined with Berlin criteria as (3);

- Respiratory distress that occurs or worsens within 7 days
- Radiological volume overload, bilateral opacities that cannot be explained by lobar or lung collapse or nodules
- Respiratory failure that cannot be explained by heart failure or fluid overload alone
- Hypoxemia
- Mild ARDS: 200 mmHg partial pressure of arterial oxygen to fraction of inspired oxygen ratio ( $\text{PaO}_2/\text{FiO}_2$ )  $\leq 300$  mmHg (PEEP  $\geq 5$  cmH<sub>2</sub>O)
- Moderate ARDS:  $100 \text{ mmHg} < \text{PaO}_2 / \text{FiO}_2 \leq 200$  mmHg (PEEP  $\geq 5$  cmH<sub>2</sub>O)
- Severe ARDS:  $\text{PaO}_2 / \text{FiO}_2 \leq 100$  mmHg (PEEP  $\geq 5$  cmH<sub>2</sub>O)

## Management of Acute Respiratory Distress Syndrome due to COVID-19 (4-8)

Hypoxemic respiratory failure develops rapidly in the course of severe COVID-19 infection and it should be recognized early. The number of breaths  $> 30$  /min, O<sub>2</sub> Sat  $< 93\%$  in the room air and heart rate  $> 120$  beats/min are important parameters in evaluating the respiratory failure in these patients. They have increase in respiratory workload and increase in hypoxemia despite conventional oxygen therapy either with nasal cannula or Venturi mask. Besides conventional oxygen therapy the prone position in non-intubated patients with lung involvement has been shown to have positive effects on hypoxia. Additionally, high flow nasal oxygen therapy and noninvasive mechanical ventilation support can be applied cautiously to selected hypoxemic respiratory failure cases, if possible within negative pressure rooms due to risk of viral transmission. The use of noninvasive positive pressure ventilation should preferably be restricted to patients with COVID-19 who have respiratory insufficiency due to chronic obstructive pulmonary disease cardiogenic pulmonary edema, or obstructive sleep apnea rather than ARDS. But, these patients should be followed closely for clinical worsening, if there is no positive response within the first

hour (refractory hypoxemia, follow-up, tidal volume > 9 ml / ideal body weight), patients should be evaluated for intubation and invasive mechanical ventilation.

In patients developing ARDS clinic, it is recommended to apply a lung protective mechanical ventilation strategy with low tidal volumes (4-8 ml / ideal body weight) and low inspiratory pressures (plateau pressure <30 cmH<sub>2</sub>O); the number of breaths can be increased up to 35 breaths / min if needed. In case of uncontrolled side effects and when pH becomes <7.15, the tidal volume can be increased to 8 ml / ideal body weight (kg). Otherwise permissive hypercapnia may be allowed. PEEP (end-expiratory positive pressure) titration is recommended at pressures that will prevent atelecto- trauma and provide alveolar clearance but will not cause overstress. If compliance is good in intubated patients (static > 40 mL / cmH<sub>2</sub>O), recruitment and high PEEP values may not be required. However, high PEEP administration is recommended in patients with moderate and severe ARDS (patients undergoing > 10 cmH<sub>2</sub>O PEEP should be followed for barotrauma). If hypoxemia deepens, if PaO<sub>2</sub> / FiO<sub>2</sub> ratio is <100-150 mmHg; PEEP 2-3 cm H<sub>2</sub>O is increased in every 15-30 minutes and O<sub>2</sub> Sat is kept in the range of 88-90%. Attention is paid to the target of keeping plateau pressure <30 cmH<sub>2</sub>O. Driving pressure (plateau pressure-PEEP) around 13-15 cm H<sub>2</sub>O can also be used as a criterion. Measuring trans-pulmonary pressure by placing the esophageal balloon catheter in moderate-to-severe obese patients may be important for optimal PEEP adjustment. Recruitment maneuvers can be tried in COVID-19 ARDS patients whose hypoxemia continues despite optimal ventilation. Although recruitment maneuvers are generally not very successful, moderate pressures can be applied for approximately 30 cmH<sub>2</sub>O for 20-30 seconds, during which time the hemodynamics are closely monitored. If the patient's oxygenation or driving pressure does not improve and if the patient develops hypotension or barotrauma recruitment maneuvers should be terminated.

Sedation and neuromuscular (NM) agent can be used within the first 24-48 hours, but excessive sedation should generally be avoided. Intermittent NM blocker boluses should be preferred to continuous infusion in mechanically ventilated patients due to moderate to severe ARDS. In case of persistent ventilator asynchrony, prone ventilation, or high plateau pressure, continuous NM blockers can be applied for up to 48 hours.

In moderate to severe ARDS cases (PaO<sub>2</sub> / FiO<sub>2</sub> <150), it is recommended to apply ventilation at prone position daily for 12-16 hours. If there are no tissue hypo perfusion findings, conservative fluid support is recommended. It is important to adjust fluid balance to reduce pulmonary edema. It is recommended to stay at 500 ml-1 lt negative. In case of shock, especially in the presence of acute renal failure and oliguria, the fluid balance can be achieved together with renal replacement therapy.

The routine use of inhaled NO (nitric oxide) is not recommended in COVID-19 ARDS patients. If hypoxemia persists despite optimal ventilation and salvage treatments in severe ARDS COVID-19 patients, the use of inhaled pulmonary vasodilator (inhaled 5-20 ppm NO) can be tried. If oxygenation does not improve rapidly, treatment should be reduced and discontinued. Despite lung protective ventilation, extracorporeal life support (ECMO) may be considered in patients with refractory hypoxemia, and appropriate patients should be referred to experienced centers.

## Conclusion

COVID-19 is a new infection with unresolved pathophysiological mechanisms. So there is uncertainty in terms of treatment. For ARDS treatment, intensivists must evaluate pulmonary mechanics carefully and provide lung protective mechanical ventilation with close monitorization of hemodynamics and oxygenation. As also recommended for routine ARDS treatment, for COVID-19 patients, the prone ventilation and intermittent NM blocker use should be considered at first place.

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